REMARKS

I. Introduction

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 1-14, 18-21, 27-30 and 35-51 are requested to be cancelled. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

Claim 52 is being added. Support for newly added claim 52 is found in the specification on page 17, line 9.

Claims 15, 17, 22, 23, 26, 31, and 32 are currently being amended. Support for the amendments are found throughout the specification. *See, e.g.,* page 13, lines 13-28 and page 18, line 19.

A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

Upon entry of this Amendment, claims 15-17, 22-26, 31-34 and 52 will remain pending in the application.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

II. Response to Issues Raised by Examiner in Outstanding Office Action

a. Claim Rejections - 35 U.S.C. § 103

Claims 15-20, 22-29 and 31-34 remain rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Suter *et al.* (Vaccine 1999, Vol. 96, No. 22, pp. 12697-13702) in view of Hilliard et al. (Arch Virol. 1989, Vol. 109, No. 102, pp. 83-102). The Examiner

asserts that although the viral gene of Suter *et al.* is larger than 50 kilobases, it would have been obvious for a person with ordinary skill in the art to use a smaller genomic fragment in the DNA vaccine of Suter *et al.* because Suter *et al.* already approve that a larger genomic fragment of HSV is able to induce an immune response as a DNA vaccine. Applicants respectfully disagree and request reconsideration and withdrawal of the rejection.

Claims 18-20 and 27-29 have been cancelled. Therefore, the rejection of these claims is moot.

With respect to claims 15-17, 22-26 and 31-34, solely to expedite prosecution, Applicants have amended claim 15 to recite that the vector constructs carry non-overlapping HSV genomic DNA fragments and encode two or more, but not all, of the HSV viral proteins. Support for these amendments are found throughout the specification. *See, e.g.*, page 18, line 19.

To establish a *prima facie* case of obviousness, there needs to be (1) some suggestion or motivation to modify the reference or to combine reference teachings, (2) a reasonable expectation of success, and (3) the prior art references, when combined, must teach or suggest all the limitations of the claimed invention. *See* MPEP §2143 (Aug. 2001). "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Applicants respectfully assert that the examiner has not met his burden.

The combined teachings of Suter *et al.* and Hillier et al. fail to teach or suggest all of the limitations of the claimed invention, as amended. Suter *et al.* fails to teach or suggest the claimed invention because the only region of the HSV genome deleted in Suter *et al.* are the non-coding packaging signals, meaning that the viral genome contains all of the normal coding sequences of the virus. The thrust of Suter *et al.* is to express all of the viral proteins to as closely mimic viral infection as possible. This is highlighted at page 12702, left hand column, final paragraph of Suter *et al.*, where it is stated that:

> "*The prototype BAC-VAC described in this report contains a 150-kb modified HSV-1 genome that is replication competent in mammalian cells and expresses at least all of the 36 viral genes that are essential for HSV-1 replication, but does not produce infection progeny virus*". [emphasis added]

This is also evident from the abstract of Suter *et al.* which states that:

> "*A safe modification of fHSV, fHSVΔpac, does not give rise to progeny virus because the signals necessary to package DNA into virions have been excluded. However, in mammalian cells fHSVΔpac DNA can still replicate, express the HSV-1 genes, cause cytotoxic effects, and produce virus-like particles*".

It would be counterintuitive for the skilled person to reduce the size of the fHSVΔ pac construct by two-thirds and deleting large numbers of genes. Such an approach would be contrary to the teaching of Suter *et al.* which aims to mimic infection as closely as possible. As highlighted at page 19, lines 29 to page 20, line 2 of the present application expressing all of the genes of a virus is a undesirable because some viral proteins can inhibit immune responses and/or be immunodominant decreasing the chances of eliciting a protective immune response.

Suter *et al.* directs the use of a construct to express as many of the viral proteins as possible. Therefore, Suter *et al.* teaches away from the present invention which employs much smaller regions that express the desired antigens in their natural context. The constructs of the present invention express a smaller, defined subset of antigens and are not intended to cause cytopathic effects and produce virus-like particles. Indeed they do not comprise enough of the genome of the pathogen to be able to do so. The present claims refer to size ranges for the fragments of from 5 to 25 kb for a plasmid and 25 to 50 kb for a cosmid, which is well under half of the 150 kb HSV genome. Since the claimed constructs carry well under half of the HSV genome, they are distinct from the construct in Suter *et al.* which carries virtually all of the HSV genome.

The Examiner's attention is also drawn to Example 1 of the present application, and in particular to page 46, lines 6 to 16, which indicates that the immune response seen with the constructs of the present invention comprising genomic fragments is unexpectedly superior to that seen with a plasmid comprising only the antigen coding sequences and none of the

accompanying genomic sequences. Thus, not only do the constructs of the invention not suffer from the problems of viral vectors that express all of the proteins of a virus, but they are also superior to vectors which express isolated antigen coding sequences.

The teachings of Hillier *et al.* do not cure the deficiencies of Suter *et al.* Therefore, the claimed invention is not obvious over the combined teachings of Suter *et al.* and Hillier *et al.*

b. Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 15-20, 22-29 and 31-34 are rejected by the Examiner under 35 U.S.C. § 112, first paragraph for lack of written description. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that Applicants do not have possession for more than one vectors to deliver more than one pathogen's DNA fragments having at least 80% homology to a virus genomic fragment or a DNA fragment hybridizing to the virus genomic DNA. Office Action at page 3. Applicants respectfully disagree. However, to expedite prosecution, Applicants have amended part (a) of claim 15 to recite "providing a core carrier coated with vector constructs carrying non-overlapping HSV genomic DNA fragments" and have deleted subparts (i)-(iii).

Additionally, in item 14 of the outstanding Office Action, the Examiner refers to the regions encoding the gB and gD antigens of HSV being 1182 and 2110 bp respectively, and argues that the application does not describe any big fragments from 5 to 50 kb carried by plasmids and cosmids as specified by the claims. However, while the coding regions of gB and gD are the specificed sizes, the actual fragments carried in the vectors used in the Examples are both over 5 kb. Applicants direct the Examiner's attention to Example 1, page 46, lines 6 to 10, in which a cosmid containing genomic fragment # 68 is employed. As is shown by Figure 1, the size of fragment #68 is well in excess of 5 kb. In addition, Applicants direct the Examiner's attention to Example 2, at page 47, first paragraph, which illustrates that the two PCR fragments of the HSV genome amplified and cloned into plasmids are 5.2

and 8.5 kb in size and are therefore in excess of the 5 kb lower size limit specified by the claims.

For the reasons discussed above, the claims, as amended are fully supported by the specification and complies with the written description requirements of 35 U.S.C. § 112, first paragraph.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By _____

FOLEY & LARDNER LLP
Customer Number:
22428
PATENT TRADEMARK OFFICE
Telephone: (202) 672-5483
Facsimile: (202) 672-5399

Richard C. Peet
Attorney for Applicant
Registration No. 35,792